UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,991	09/16/2003	Leonard F. Bjeldanes	09272-0013001	4613

26181 7590 02/24/2010

FISH & RICHARDSON P.C.
PO BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
BETTON, TIMOTHY E	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
02/24/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/664,991	BJELDANES ET AL.	
	Examiner	Art Unit	
	TIMOTHY E. BETTON	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,7-15 and 20-22* is/are pending in the application.

4a) Of the above claim(s) *8-14 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2, 7, and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Remarks filed on 8 September 2009 have been acknowledged and duly made of record.

Applicants' disclose [that] [w]ithout acquiescing to the Examiner's rejections, and solely the purpose of expediting prosecution, claim 1 is amended to recite a method comprising contacting a human patient determined to be subject or predisposed to an androgen-dependent pathology selected from the group consisting of prostate hyperplasia, acne, androgenetic alopecia and hirsutism with an effective amount of an antiandrogenic, optionally substituted 3,3'-diindolylmethane (DIM); and detecting a reduction in the pathology or progress of the pathology. Neither Farley nor Safe disclose or suggest treating a patient determined to be subject or predisposed to prostate hyperplasia, acne, or androgenetic alopecia and hirsutism. Further, neither Farley nor Safe disclose or suggest or detecting a reduction in the pathology or progress of the pathology of prostate hyperplasia, acne, androgenetic alopecia and hirsutism. As such, the present claims are clearly patentable over Farley and Safe and the rejections based on such should be withdrawn. Accordingly, Applicants respectfully request immediate allowance of the claims.

Applicants argument/amendment is considered but is not found persuasive because the limitations within the current amendment of claim 1 drawn to a human patient determined to be subject or predisposed to an androgen-dependent pathology does not overcome the rejections of record. The reason is that the target population is broad in view of applicants' disclosure. A subject predisposed to an androgen-dependent pathology could virtually be anyone. The art is

replete with variable factors (i.e., genetic, environmental, developed, etc) which could contribute to this alleged novel limitation.

Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 1-2, 7, and 15 are pending further prosecution on the merits. Claims 3-6 and 16-19 are cancelled. Claims 8-14 and 20-22 are withdrawn from further consideration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 (e) that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an

international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-2, 7, and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Farley (USPN 6544564 B1).

Principally, Farley teaches [a]n inventive and proprietary formula to enhance the body's natural immune function against viral and infectious diseases and cancer (Abstract only).

Farley teach an immunity system of a human body, against viral and infectious disease and cancer (col. 1, lines 1 and 2).

Further, Farley teaches [that] [t]hese all natural formulas contain phytochemicals that have been shown to cause cell apoptosis, cytotoxicity and inhibition of replication in all of the following cancer cell lines. TBP-1 human monocytic leukaemia cells CaCo-2 human colon cancer cells Human leukaemia HL-60 cells HLA B40-positive breast cancer cells Estrogen receptor positive MCF-7 (human breast cancer cell lines) Estrogen receptor negative MDA-MB-468 (human breast cancer cell lines) Squamous cell carcinoma (SCC) (oral) Androgen-sensitive LNCaP (human prostate) Androgen-insensitive PC-3 cell lines (human prostate)(col. 1 , lines 43-57).

Accordingly, Farley discloses DIM with a range of milligram concentration (col. 1, line 20) (col. 2, line 30-32 and 35).

Based upon the subject matter of Farley *supra,* the inherency is evident with regard to a treatment for cancer. Accordingly, DIM is disclosed in a range of dosages which is clearly anticipatory with regard to treatment. As also disclosed *supra*, Androgen-insensitive PC-3 cell

lines is listed as a cancer. Observation of therapeutical effect would have been inherent for a therapeutical method.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 7, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by (Safe USPGPUB 2002/0115708 A1).

Safe essentially teach [that] [t]he DIM series of compounds containing both ring and methylene -C substituents can be used for treating **multiple cancers** through both Ah receptor-dependent and independent pathways. […]. ***We also investigated the induction of EROD activity in two additional androgen-responsive prostate cancer cell lines. The results illustrated in FIG. 13 show that 0.1 to 10 nM TCDD induced ERODactivity in androgen-responsive 22 Rv1 prostate cancer cells (top), and DIM also induced a minimal (but significant) increase in ERODactivity (middle). In combination studies, higher concentration of DIM inhibited TCDD induced activity, and this is consistent with results of previous studies which show that DIM interacts directly with CYP1A1 protein and inhibits catalytic activity such as EROD***[…]. Thus, human prostate cancer cells express a functional Ah receptor [0071].

Further, Safe teaches methods and compositions for the treatment of a wide array of cancers and tumors. In illustrative embodiments, diindolylmethanes, C-substituted diindolylmethanes, and analogs thereof have been described, which when administered either alone, or in combination with other anti-cancer or anti-tumorigenic compounds, provide new therapies for the treatment of prostate cancer (Abstract, [0050], last line of instant paragraph).

Safe teaches administration (in vitro and in vivo) to human patients in need thereof via inhibition of prostate cancer cell growth which includes androgen-sensitive and androgen-responsive (including androgen-sensitive, or androgen-responsive) [0065, 0049, 0071].

Safe discloses the directed use of DIM and derivatives thereof for the specific contacting, detecting, and inhibiting via a gel mobility shift assay for prostate cancer cells (Brief description of Drawings – Table CWU – DRTL (1)) in a comparative study to estrogen-dependent pathologies. **Safe further discloses the methods of administering said antiandrogenic agent in claims 16, 34, 51, and 69, therein.**

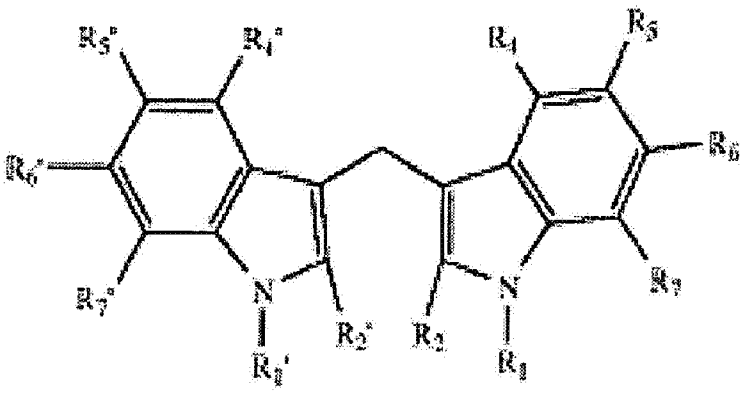
Safe teaches derivatives of the DIM core structure that are also taught in the instant application. In said referenced publication on page 3, section [0039] under the heading: Definitions, said structure is disclosed. Derivatives of the core structure are disclosed in the instant application on page 3 of the specification under the heading: Summary of Invention. Safe discloses in published claims, the *in vitro* method (by use of assays which are disclosed empirical series of method steps used to detect a reaction) **of treating cancer**, the method comprising obtaining a mammal comprising cancer cells, and administering to the mammal a composition comprising an effective dose of a compound of the said formula. Claims 17-19 are made obvious over claims 16, 34, 51, and 69 in Safe obvious over using this related core structure in the use of treatment against the specific cancer-types, i.e., **prostate cancer** and pathologies thereof.

Safe teaches detection on page 5, Example 2, section [0058] in that a process is disclosed where inhibition was determined, i.e., where clear proliferation of cancer cell lines were significantly inhibited. Further, detection is implied in said reference where sensitive cells were noticeably inhibited at the lowest concentration.

Safe, in accordance, more specifically teaches detection on page 4, section [0047] of said referenced publication where resolution of the mixture using chiral chromatography column would result in the isolation of purified or pure enantiomers products. Furthermore, Safe teaches the use of thin-layer chromatography and liquid chromatography in section [0067] (page 6), both well-established detection methods and/or detection facilitators.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to consider the teachings of Safe et al. in obviousness over the claimed invention.

Essentially, Safe et al. teach the scope and content which encompasses the scope and content of the claimed invention. Principally, the scope is drawn to a method of providing an antiandrogen to a host determined to be in need thereof. Safe et al. teach the claimed compound and/or derivative thereof to be used in the administration of androgenic disorders. Safe et al. teach an in vitro method of treating cancer cells with a compound of formula:



(Please see claim 1 and 36 of Safe et al., page 9 and 11, respectively, (para 90)).

Accordingly, the second step of the current invention does not carry much patentable weight because detecting a resultant antiandrogenic response in the host would reasonably occur due to such a method of administration. Contacting the host with an effective amount of DIM which is an active agent (drug) is art-known to change the molecular physiology of the body. Thus, the limitation directed to detecting is anticipated by any form of administration involving an active agent such as DIM.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627